REMARKS

Claim Amendments:

Claims 1 and 11 have been amended to correct a typographical error by replacing the recitation "with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of" with the recitation "with 1 to 3 substituents selected from the group consisting of" in definitions of B and C groups.

Claims 1 and 11 have been further amended to add the recitation "alkenyloxy, substituted alkenyloxy" in the definition of B group. Support for this amendment can be found at page 9, lines 24 and 29 and page 10, lines 19-20 and lines 27-28.

Claims 1 and 11 have been yet further amended to replace the recitation "and pharmaceutically acceptable salts thereof" with the recitation "or pharmaceutically acceptable salts thereof."

Claim 11 has been yet further amended to correct a typographical error by deleting "or C" from the recitation "in addition to ring B or C."

Claims 2 and 13 have been amended to correct a typographical error by deleting "the" from the recitation "further the wherein."

Claims 8-10 and 17-21 have been amended by re-writing in proper form in order to provide reference to precedent claims in the alternative only and avoid dependence on another multiple dependent claim either directly or indirectly.

New Claims 22-27 have been added. Support for these claims can be found in the originally-filed Claims 20 and 21.

Accordingly, no new matter was added by way of these amendments. The Examiner is hereby requested to enter these amendments.

A marked up version of the previous version of claims and a clean version of the entire set of the pending claims are attached.

Rejections Under 35 U.S.C. § 112

1. Claims 1-7 and 11-16

Claims 1-7 and 11-16 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

a. The Office Action asserts that Claim 1 is ambiguous because the recitation "and pharmaceutically acceptable salts thereof" suggests a mixture of compounds and salts. Complying with the Examiner's advice, Applicants have replaced "and" with "or." Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

b. The Office Action asserts that it is unclear how many substituents are intended in groups B and C of Claims 1 and 11 which recite the phrase "with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of." Claims 1 and 11 have been amended to correct a typographical error by replacing the recitation "with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of" with the recitation "with 1 to 3 substituents selected from the group consisting of" in definitions of B and C groups. Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

c. The Office Action asserts that the phrase "further the wherein" in Claims 2 and 13 seems incomplete. Claims 2 and 13 have been amended to correct a typographical error by deleting "the" from the recitation "further the wherein." Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

d. The Office Action asserts that Claims 2-5 lack antecedent basis because they recite "alkenyloxy" and/or "substituted alkenyloxy" as a substituent for ring B, which are not recited in Claim 1. Claim 1 has been amended to add the recitation "alkenyloxy, substituted alkenyloxy" in the definition of B group. Support for this amendment can be found at page 9, lines 24 and 29 and page 10,

lines 19-20 and lines 27-28. Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

e. The Office Action asserts that it is unclear as to relationship of ring C with formulae IIa-IIe because Claim 11 recites the phrase "in addition to ring B or C," while ring C does not appear in formulae Iia-IIe. Claim 11 has been amended to correct a typographical error by deleting "or C" from the recitation "in addition to ring B or C." Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

f. The Office Action asserts that Claims 13-16 lack antecedent basis because they recite "alkenyloxy" and/or "substituted alkenyloxy" as a substituent for ring B, which are not recited in Claim 11. Claim 11 has been amended to add the recitation "alkenyloxy, substituted alkenyloxy" in the definition of B group. Support for this amendment can be found at page 17, lines 28 and 33; and page 18, lines 23-24 and lines 31-32. Accordingly, this rejection is overcome. Withdrawal of the rejection is requested.

g. Claims 6, 7 and 12 stand rejected as being dependent on Claim 1 or 11. In light of the above-mentioned amendments to Claims 1 and 11, Applicants request the withdrawal of this rejection.

2. Claims 1, 4-7, 11, 12, 15 and 16

Claims 1, 4-7, 11, 12, 15 and 16 stand rejected under 35 U.S.C. § 112, First Paragraph, as being not enabling for compounds with ring B or C as a bicycle or tricycle, i.e., fused pyridone or fused pyrimidone. This rejection is respectfully traversed.

Under 35 U. S. C. § 112, all that is required is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. Thus, the specification must teach one skilled in the art how to make and use a compound with ring B or C as a fused ring. The test of enablement is whether one

reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. In re Wands, 858 F.2d 731 (Fed. Cir. 1988); United States v. Telectronics, Inc., 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01.

The law clearly states that "a considerable amount of experimentation is permissible, if it is merely routine." In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Further, the fact that experimentation may be complex does not necessarily make it undue. Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104 (Fed. Cir. 1985); In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Thus, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, is it undue. In re Angstadt, 537 F.2d 498 (CCPA 1976).

The outstanding Office Action has questioned the "how to make" enablement requirements of the First Paragraph of 35 U.S.C. §112. Specifically, the Office Action has asserted that the specification, while being enabling for compounds with ring B or C as a monocycle (i.e., pyridone or pyrimidone), does not provide a generic teaching to make compounds with ring B or C as a fused ring.

Contrary to the Office's assertion, in addition to compounds with ring B or C as a monocycle, the specification does provide teachings for preparing compounds with ring B or C as a fused ring. Specifically, the specification describes the methods for preparing compounds with ring B or C as a fused ring on page 59, line 23 through page 60, line 18, as follows:

"The procedures of Shiotani et al. (*J. Org. Chem.* **1997**, 34(3), 941-952) could be used to prepare a pyridin-2-one fused via the 4 and 5 positions with a tetrahydrofuran. Following methods described in the working examples, this compound could be elaborated into a 1-methyl-3-iodopyridin-2-one fused via the 4 and 5 positions with a tetrahydrofuran. As described above, this compound could be applied in a palladium catalyzed coupling with a suitably protected pinacolatoborono phenylalanine or a suitably protected pinacolatoborono heteroarylalanine.

The procedures of Adembri (*J. Chem. Soc. Perkin Trans*. 1. **1975**, 2190-2194) could be used to prepare a pyridin-2-one fused via the 4 and 5 positions with an isoxazole. Following methods described in the working examples, this compound could be elaborated into a 1-methyl-3-iodopyridin-2-one fused via the 4 and 5 positions with an isoxazole. As described above, this compound could be applied in a palladium catalyzed coupling with a suitably protected pinacolatoborono phenylalanine or a suitably protected pinacolatoborono heteroarylalanine.

The procedures of Dorofeenko et al. (*Khim. Geterotsikl. Soedin*. **1976**, 533) could be used to prepare a pyridin-2-one fused via the 4 and 5 positions with a furan. Following methods described in the working examples, this compound could be elaborated into a 1-methyl-3-iodopyridin-2-one fused via the 4 and 5 positions with an isoxazole. As described above, this compound could be applied in a palladium catalyzed coupling with a suitably protected pinacolatoborono phenylalanine or a suitably protected pinacolato heteroarylalanine."

The Office Action has further alleged that the specification does not disclose how the starting material for a fused pyridone or fused pyrimidone can be made or obtained. However, these starting materials are defined by the definition of the various heterocycle terms in Applicants' specification. It is submitted that the preparation of these starting materials are well within the scope of one having ordinary skill in the art using existing procedures or obvious modifications thereof and in many cases the starting materials are commercial materials. Thus, it is submitted that Applicants' specification fully meets the "how to make" enablement requirements of the First Paragraph of 35 U.S.C. §112.

One reference has been cited as state of the art at the time the application was filed, Head et al. WO 99/37618. Head et al., it is asserted, does not provide preparation for compounds of fused pyridone or fused pyrimidone, nor does it relate said compounds to the inhibition of VLA-4. Lack of teachings in the Head et al. reference in regard to the claimed compounds of the present invention is asserted as evidencing a burden of undue experimentation on one of skill in the art, in practicing the claimed invention.

Although Applicants agree with the Examiner' assertion that Head et al. does not teach compounds of the present invention, Applicants still maintain that this reference is irrelevant here because, as discussed above, the specification by its own terms provides considerable guidance to enable a skilled artisan to make and use a compound with ring B or C as a fused ring.

In conclusion, based on the arguments presented above, there is ample support for the specification being fully enabling. Accordingly, Applicants respectfully request that the 35 U.S.C. § 112, First Paragraph, rejections be withdrawn.

Claim Objections:

Claims 8-10 and 17-21 stand objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to precedent claims in the alternative only, and must not depend on another multiple dependent claim either directly or indirectly.

In accordance with MPEP § 608.01(n), Claims 8-10 and 17-21 have been amended by re-writing them in proper form in order to provide reference to precedent claims in the alternative only and avoid dependence on another multiple dependent claim either directly or indirectly.

Accordingly, this objection is overcome. Withdrawal of the objection is requested.

Conclusions:

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Early allowance of the claims of this application is earnestly solicited.

Respectfully submitted,
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

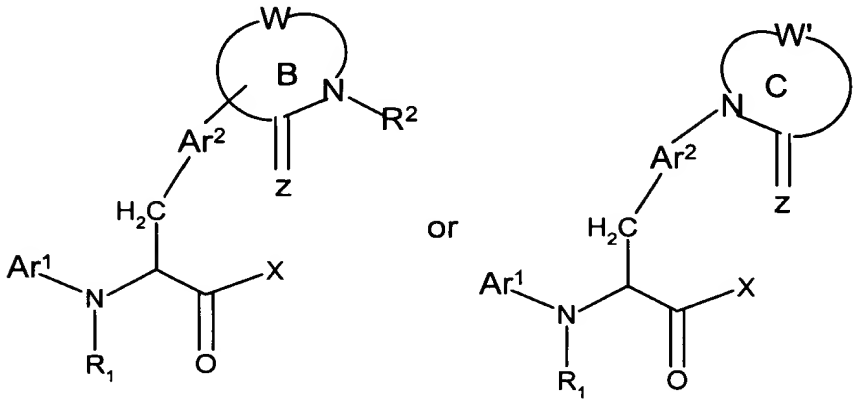
Date: 04.01.03 By: Galina Yakovleva

Galina M. Yakovleva, Ph.D.
Registration No. 47,192

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

MARKED-UP COPY OF AMENDED CLAIMS

1. (Amended) A compound (Ia) or (Ib):



(Ia) (Ib)

wherein:

Ar^1 is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-

substituted aryl, -$OS(O)_2$-heteroaryl, -$OS(O)_2$-substituted heteroaryl, -$OS(O)_2$-heterocyclic, -$OS(O)_2$-substituted heterocyclic, -OSO_2-NRR where each R is independently hydrogen or alkyl, -$NRS(O)_2$-alkyl, -$NRS(O)_2$-substituted alkyl, -$NRS(O)_2$-aryl, -$NRS(O)_2$-substituted aryl, -$NRS(O)_2$-heteroaryl, -$NRS(O)_2$-substituted heteroaryl, -$NRS(O)_2$-heterocyclic, -$NRS(O)_2$-substituted heterocyclic, -$NRS(O)_2$-NR-alkyl, -$NRS(O)_2$-NR-substituted alkyl, -$NRS(O)_2$-NR-aryl, -$NRS(O)_2$-NR-substituted aryl, -$NRS(O)_2$-NR-heteroaryl, -$NRS(O)_2$-NR-substituted heteroaryl, -$NRS(O)_2$-NR-heterocyclic, -$NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, -$N[S(O)_2\text{-}R']_2$ and -$N[S(O)_2\text{-}NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^1 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Ar^2 is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, aminoacyl, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

Z is -O- or -S-;

B is a group wherein W, together with -C(=Z)NR^2-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO$_n$- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of [with one or two substituent(s) selected from the group consisting of] hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkenyloxy, substituted alkenyloxy;

R^2 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

C is a group wherein W', together with -C(=Z)N-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO$_n$- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl,

heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of [with one or two substituent(s) selected from the group consisting of] hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, alkylenedioxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, nitro, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR″R″ where each R″ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diasteromers [and] or pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula I has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

2. (Amended) The compound of Claim 1 wherein (Ia), B is a group wherein W, together with -C(=Z)NR^2- where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further [the]

wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

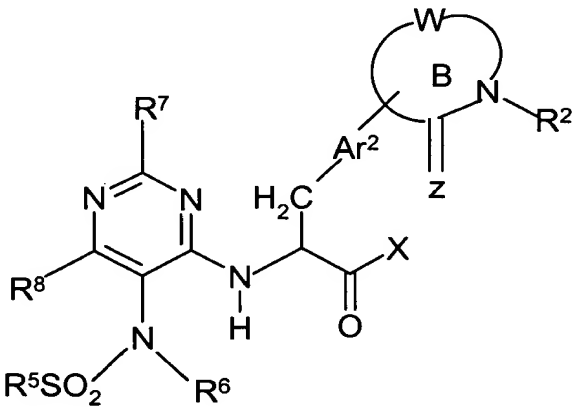
8. (Amended) The compound as in one of Claims [2] 1 to 7 wherein Ar^2 is phenyl.

9. (Amended) The compound as in one of Claims 1 to 7 wherein X is hydroxyl and R^1 is hydrogen.

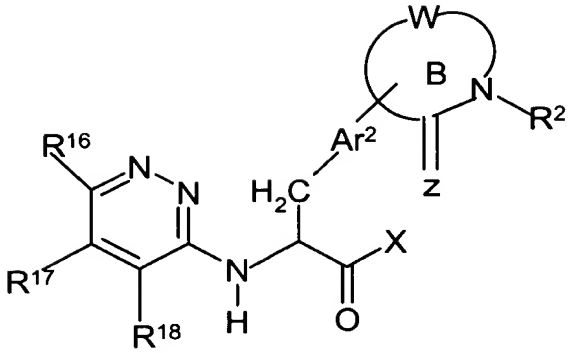
10. (Amended) The compound as in one of Claims [8] 1 to 7 wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.

11. (Amended) The compound of Claim 1 wherein the compound has formula IIa, IIb, IIc, IId, or IIe:

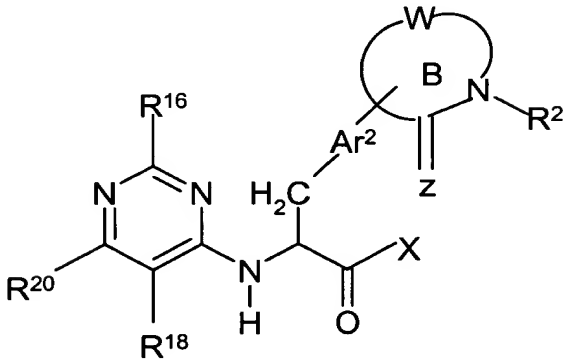
IIa



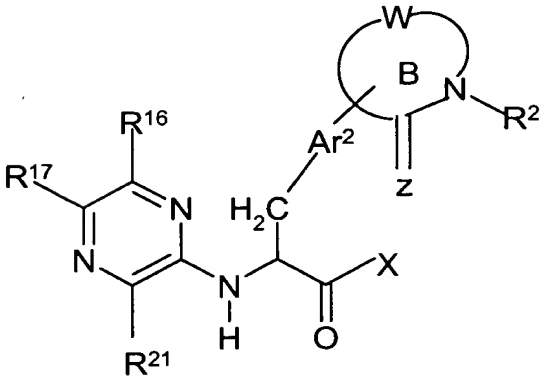
IIb


W
B
N
R2
Ar2
z
R16
N
N
H2C
X
R17
N
H
O
R18

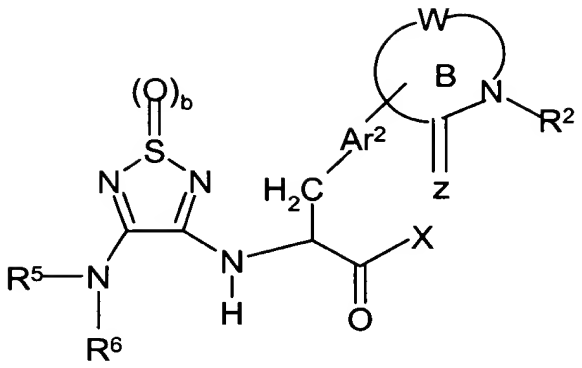
IIc


W
B
N
R2
R16
Ar2
z
N
N
H2C
X
R20
N
H
O
R18

IId


W
B
N
R2
R16
Ar2
z
R17
N
H2C
N
X
N
H
O
R21

IIe



wherein

X is hydroxyl or alkoxy;

Ar^2 is an aryl or heteroaryl group optionally substituted, in addition to ring B [or C], with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic,

substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO_2R^{10} where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

B is a group wherein W, together with -C(=Z)NR^2-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO_n- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl,

heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of [with one or two substituent(s) selected from the group consisting of] hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkenyloxy, substituted alkenyloxy;

R^2 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl; and

and enantiomers, diastereomers [and] or pharmaceutically acceptable salts thereof.

13. (Amended) The compound of Claim 11 wherein B is a group wherein W, together with $-C(=Z)NR^2-$ where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further [the] wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

17. (Amended) The compound as in any one of Claims 11 to 16 wherein Ar^2 is phenyl.

18. (Amended) The compound as in any one of Claims 11 to 16 wherein X is hydroxyl and R^1 is hydrogen.

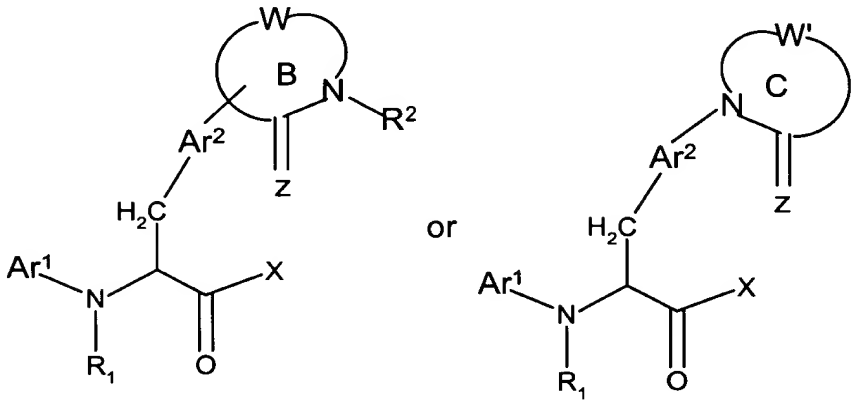
19. (Amended) The compound as in any one of Claims 11 to 16 [18] wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.

20. (Amended) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 [to 19] or 11-16.

21. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 [to 19] or 11-16.

CURRENTLY PENDING CLAIMS 1-27

1. (Amended) A compound (Ia) or (Ib):



(Ia) (Ib)

wherein:

Ar^1 is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, $-OS(O)_2$-alkyl, $-OS(O)_2$-substituted alkyl, $-OS(O)_2$-aryl, $-OS(O)_2$-

substituted aryl, -$OS(O)_2$-heteroaryl, -$OS(O)_2$-substituted heteroaryl, -$OS(O)_2$-heterocyclic, -$OS(O)_2$-substituted heterocyclic, -OSO_2-NRR where each R is independently hydrogen or alkyl, -$NRS(O)_2$-alkyl, -$NRS(O)_2$-substituted alkyl, -$NRS(O)_2$-aryl, -$NRS(O)_2$-substituted aryl, -$NRS(O)_2$-heteroaryl, -$NRS(O)_2$-substituted heteroaryl, -$NRS(O)_2$-heterocyclic, -$NRS(O)_2$-substituted heterocyclic, -$NRS(O)_2$-NR-alkyl, -$NRS(O)_2$-NR-substituted alkyl, -$NRS(O)_2$-NR-aryl, -$NRS(O)_2$-NR-substituted aryl, -$NRS(O)_2$-NR-heteroaryl, -$NRS(O)_2$-NR-substituted heteroaryl, -$NRS(O)_2$-NR-heterocyclic, -$NRS(O)_2$-NR-substituted heterocyclic where R is hydrogen or alkyl, -$N[S(O)_2\text{-}R']_2$ and -$N[S(O)_2\text{-}NR']_2$ where each R′ is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^1 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Ar^2 is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, aminoacyl, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

Z is -O- or -S-;

B is a group wherein W, together with -C(=Z)NR^2-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO$_n$- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkenyloxy, substituted alkenyloxy;

R^2 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

C is a group wherein W', together with -C(=Z)N-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO$_n$- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further

wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, alkylenedioxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, nitro, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR″R″ where each R″ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diasteromers or pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula I has a binding affinity to VLA-4 as expressed by an IC_{50} of about 15μM or less.

2. (Amended) The compound of Claim 1 wherein (Ia), B is a group wherein W, together with -C(=Z)NR^2- where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1

or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

3. The compound of Claim 1 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl, or 6-pyrimidon-5-yl that is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

4. The compound of Claim 1 wherein B is a group wherein W, together with -C(=Z)NR^2- where Z is -O-, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

5. The compound of Claim 1 wherein B is 2-pyridone or 6-pyrimidone that is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one, and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

6. The compound of Claim 1 wherein Ar^1 is heteroaryl optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

7. The compound of Claim 6 wherein Ar^1 is 1-oxo-1,2,5-thiadiazole, 1,1-dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine ring which is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

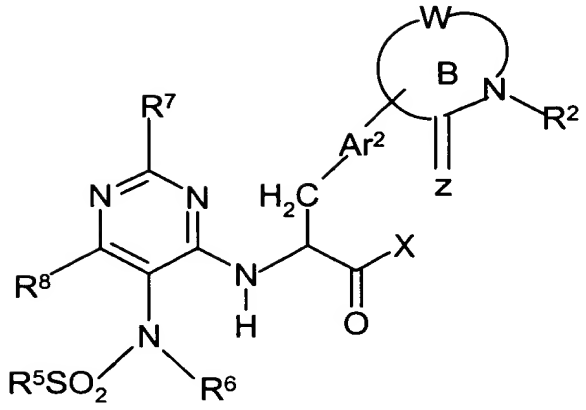
8. (Amended) The compound as in one of Claims 1 to 7 wherein Ar^2 is phenyl.

9. (Amended) The compound as in one of Claims 1 to 7 wherein X is hydroxyl and R^1 is hydrogen.

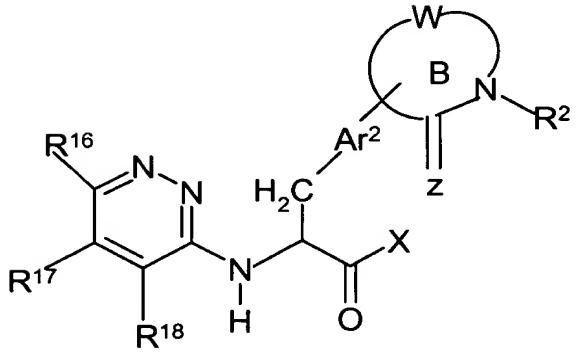
10. (Amended) The compound as in one of Claims 1 to 7 wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.

11. (Amended) The compound of Claim 1 wherein the compound has formula IIa, IIb, IIc, IId, or IIe:

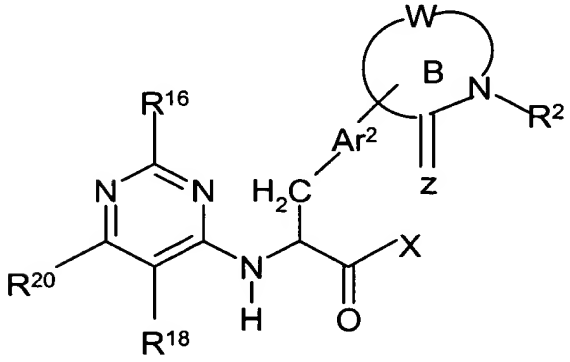
IIa

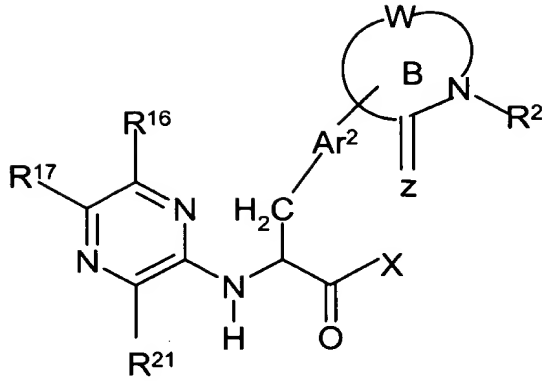

W
B
N
R2
Z
Ar2
H2C
X
O
N
H
R7
N
N
R8
N
R5SO2
R6

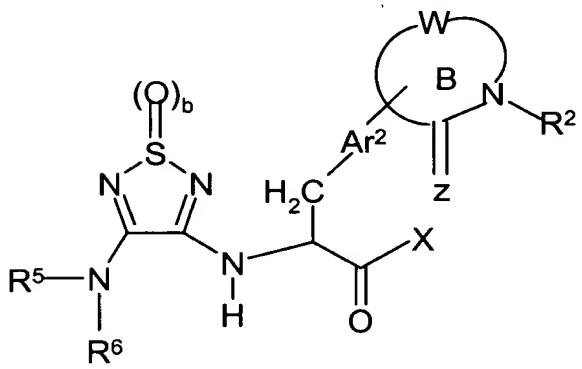
IIb


W
B
N
R2
Z
Ar2
H2C
X
O
N
H
R16
N
N
R17
R18

IIc


W
B
N
R2
Z
Ar2
H2C
X
O
N
H
R16
N
N
R20
R18

IId 

IIe 

wherein

X is hydroxyl or alkoxy;

Ar^2 is an aryl or heteroaryl group optionally substituted, in addition to ring B, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

R^5 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO_2R^{10} where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

B is a group wherein W, together with $-C(=Z)NR^2-$, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and $-SO_n-$ (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, alkenyloxy, substituted alkenyloxy;

R^2 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl; and

and enantiomers, diastereomers or pharmaceutically acceptable salts thereof.

12. The compound of Claim 11 wherein the compound is selected from formula IIc, IId or IIe.

13. (Amended) The compound of Claim 11 wherein B is a group wherein W, together with -C(=Z)NR^2- where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

14. The compound of Claim 13 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl, or 6-pyrimidon-5-yl that is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

15. The compound of Claim 11 wherein B is a group wherein W, together with -C(=Z)NR^2- where Z is -O-, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

16. The compound of Claim 15 wherein B is 2-pyridone or 6-pyrimidone that is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one, and wherein the resulting fused ring is

optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

17. (Amended) The compound as in any one of Claims 11 to 16 wherein Ar^2 is phenyl.

18. (Amended) The compound as in any one of Claims 11 to 16 wherein X is hydroxyl and R^1 is hydrogen.

19. (Amended) The compound as in any one of Claims 11 to 16 wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.

20. (Amended) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16.

21. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16.

22. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein Ar^2 is phenyl.

23. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein X is hydroxyl and R^1 is hydrogen.

24. (New) A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.

25. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein Ar^2 is phenyl.

26. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein X is hydroxyl and R^1 is hydrogen.

27. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in any one of Claims 1-7 or 11-16 wherein Ar^2 is phenyl, X is hydroxyl and R^1 is hydrogen.